Uroben™ XR

Mirabegron Tablet

Presentation
Uroben™ XR 25: Each extended release tablet contains Mirabegron INN 25 mg.
Uroben™ XR 50: Each extended release tablet contains Mirabegron INN 50 mg.

Description
Mirabegron is a beta-3 adrenergic agonist. It is a white powder. It is practically insoluble in water (0.082 mg/mL). It is soluble in methanol and dimethyl sulfoxide. Each Uroben extended-release tablet for oral administration contains either 25 mg or 50 mg of Mirabegron.

Indication and usage
Monotherapy: Mirabegron is a beta-3 adrenergic agonist indicated for the treatment of overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency, and urinary frequency.

Combination with Muscarinic Antagonist: Mirabegron in combination with the muscarinic receptor antagonist solifenacin succinate is indicated for the treatment of OAB with symptoms of urge urinary incontinence, urgency, and urinary frequency.

Dosage and administration
Monotherapy: The recommended starting dose of Mirabegron is 25 mg once daily with or without food. Mirabegron 25 mg is effective within 8 weeks. Based on individual patient efficacy and tolerability the dose may be increased to 50 mg once daily.

Combination with Muscarinic Receptor Antagonist (Solifenacin Succinate)
The recommended starting doses for combination treatment are Mirabegron 25 mg once daily and solifenacin succinate 5 mg once daily. Based on individual patient efficacy and tolerability, The Mirabegron dose may be increased to 50 mg once daily after 4 to 8 weeks.

Mirabegron and solifenacin succinate can be taken together with or without food.

Dose adjustments in specific populations
The daily dose of Mirabegron should not exceed 25 mg once daily in the following populations:
- Patients with severe renal impairment (CrCL 15 to 29 mL/min or eGFR 15 to 29 mL/min/1.73 m^2).
- Patients with moderate hepatic impairment
- Mirabegron is not recommended for use in patients with End-Stage Renal Disease (ESRD), or in patients with severe hepatic impairment.

Side-effects
Most commonly reported adverse reactions with Mirabegron monotherapy (> 2% and > placebo) were hypertension, nasopharyngitis, urinary tract infection and headache. Most commonly reported adverse reactions with Mirabegron, in combination with solifenacin succinate 5 mg (> 2% and > placebo and > comparator), were dry mouth, urinary tract infection, constipation, and tachycardia.

Contraindications
Do not use Mirabegron in patients who have known hypersensitivity reactions to mirabegron or any inactive ingredients of the tablet.

Precautions
- *Increases in blood pressure:* Mirabegron alone or in combination with Solifenacin succinate 5 mg can increase blood pressure. Periodic blood pressure determinations are recommended, especially in hypertensive patients. Mirabegron is not recommended for use in severe uncontrolled hypertensive patients.
- *Urinary retention in patients with bladder outlet obstruction and in patients taking muscarinic receptor antagonist drugs for overactive bladder:* Administer with caution in these patients because of risk of urinary retention.
- *Angioedema:* Angioedema of the face, lips, tongue and/or larynx has been reported with Mirabegron.
- *Patients taking drugs metabolized by CYP2D6:* Mirabegron is a moderate inhibitor of CYP2D6. Appropriate monitoring is recommended and dose adjustment may be necessary for narrow therapeutic index CYP2D6 substrates.

Use in specific population
Pregnant women: It is a pregnancy category C drug. There are no adequate and well-controlled studies using Mirabegron in pregnant women. Mirabegron should be used during pregnancy only if the potential benefit to the patient outweighs the risk to the patient and fetus.

Nursing mothers: Mirabegron is predicted to be excreted in human milk and is not recommended for use by nursing mothers.

Pediatric use: The safety and effectiveness of Mirabegron alone, or in combination with solifenacin succinate 5 mg, in pediatric patients has not been established.

Geriatric use: No dose adjustment is recommended for elderly patients.

Drug interaction
Drugs Metabolized by CYP2D6 (e.g., Metoprolol and Desipramine): Mirabegron is a CYP2D6 inhibitor and, when used concomitantly with drugs metabolized by CYP2D6, especially narrow therapeutic index drugs, appropriate monitoring and possible dose adjustment of those drugs may be necessary.

Digoxin: When initiating a combination of Mirabegron and digoxin with or without solifenacin succinate, prescribe the lowest dose of digoxin; monitor serum digoxin concentrations to titrate digoxin dose to desired clinical effect.

Overdosage
Mirabegron has been administered to healthy volunteers at single doses up to 400 mg. At this dose, adverse events reported included palpitations (1 of 6 subjects) and increased pulse rate exceeding 100 bpm (3 of 6 subjects). Multiple doses of Mirabegron up to 300 mg daily for 10 days showed increases in pulse rate and systolic blood pressure when administered to healthy volunteers. Treatment for over dosage should be symptomatic and supportive. In the event of overdosage, pulse rate, blood pressure and ECG monitoring is recommended.

Storage
Do not store above 30 °C. Keep away from light and out of the reach of children.

Commercial pack
Uroben™ XR 25: Each box contains 3 blister strips of 10 tablets.
Uroben™ XR 50: Each box contains 3 blister strips of 10 tablets.

Manufactured by
Incepta Pharmaceuticals Ltd
Savar, Dhaka, Bangladesh
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